

# World Journal of *Hepatology*

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**INDEXING/ABSTRACTING**

*World Journal of Hepatology* is now indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, and Scopus.

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**NAME OF JOURNAL**  
*World Journal of Hepatology*

**ISSN**  
ISSN 1948-5182 (online)

**LAUNCH DATE**  
October 31, 2009

**FREQUENCY**  
Monthly

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*World Journal of Hepatology*  
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7901 Stoneridge Drive, Suite 501,  
Pleasanton, CA 94588, USA  
Telephone: +1-925-2238242  
Fax: +1-925-2238243  
E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
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**PUBLISHER**  
Baishideng Publishing Group Inc  
7901 Stoneridge Drive, Suite 501,  
Pleasanton, CA 94588, USA  
Telephone: +1-925-2238242  
Fax: +1-925-2238243  
E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

**PUBLICATION DATE**  
February 27, 2018

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## Outcomes of kidney transplantation in patients with hepatitis B virus infection: A systematic review and meta-analysis

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**Author contributions:** Thongprayoon C, Kaewput W, Sharma K and Leeaphorn N collected the data; Thongprayoon C analyzed the data; Thongprayoon C, Sharma K, Wijarnpreecha K, Leeaphorn N, Ungprasert P, Sakhuja A and Cabeza Rivera FH interpreted the data; Thongprayoon C and Kaewput W drafted the article; Wijarnpreecha K, Ungprasert P, Sakhuja A and Cabeza Rivera FH revised the article; Cheungpasitporn W made the conception and design of the study, and critically revised the article; all the authors made the final approval of the manuscript.

**Conflict-of-interest statement:** The authors deny any conflict of interest.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Invited manuscript

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**Received:** November 28, 2017

**Peer-review started:** November 28, 2017

**First decision:** December 18, 2017

**Revised:** January 10, 2018

**Accepted:** February 5, 2018

**Article in press:** February 5, 2018

**Published online:** February 27, 2018

### Abstract

#### AIM

To assess outcomes of kidney transplantation including patient and allograft outcomes in recipients with hepatitis B virus (HBV) infection, and the trends of patient's outcomes overtime.

#### METHODS

A literature search was conducted using MEDLINE, EMBASE and Cochrane Database from inception through October 2017. Studies that reported odds ratios (OR) of mortality or renal allograft failure after



kidney transplantation in patients with HBV [defined as hepatitis B surface antigen (HBsAg) positive] were included. The comparison group consisted of HBsAg-negative kidney transplant recipients. Effect estimates from the individual study were extracted and combined using random-effect, generic inverse variance method of DerSimonian and Laird. The protocol for this meta-analysis is registered with PROSPERO (International Prospective Register of Systematic Reviews; no. CRD42017080657).

## RESULTS

Ten observational studies with a total of 87623 kidney transplant patients were enrolled. Compared to HBsAg-negative recipients, HBsAg-positive status was significantly associated with increased risk of mortality after kidney transplantation (pooled OR = 2.48; 95%CI: 1.61-3.83). Meta-regression showed significant negative correlations between mortality risk after kidney transplantation in HBsAg-positive recipients and year of study (slopes = -0.062,  $P = 0.001$ ). HBsAg-positive status was also associated with increased risk of renal allograft failure with pooled OR of 1.46 (95%CI: 1.08-1.96). There was also a significant negative correlation between year of study and risk of allograft failure (slopes = -0.018,  $P = 0.002$ ). These associations existed in overall analysis as well as in limited cohort of hepatitis C virus-negative patients. We found no publication bias as assessed by the funnel plots and Egger's regression asymmetry test with  $P = 0.18$  and 0.13 for the risks of mortality and allograft failure after kidney transplantation in HBsAg-positive recipients, respectively.

## CONCLUSION

Among kidney transplant patients, there are significant associations between HBsAg-positive status and poor outcomes including mortality and allograft failure. However, there are potential improvements in patient and graft survivals in HBsAg-positive recipients overtime.

**Key words:** Hepatitis B; Kidney transplant; Kidney; Renal transplantation; Transplantation; Meta-analysis

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**Core tip:** Hepatitis B is one of the most common infectious diseases worldwide. Despite advances in medicine, chronic hepatitis B virus (HBV) infection is currently incurable. In addition, clinical outcomes of kidney transplantation in HBV infected patients are still unclear. To further assess these outcomes, we conducted this systematic review and meta-analysis to assess patient and allograft outcomes after kidney transplantation in patients with HBV Infection. We found significant associations between HBV positive status and poor outcomes including 2.5-fold increased risk of mortality and 1.5-fold increased risk of allograft loss.

Thongprayoon C, Kaewput W, Sharma K, Wijarnpreecha K, Leeaphorn N, Ungprasert P, Sakhuja A, Cabeza Rivera FH, Cheungpasitporn W. Outcomes of kidney transplantation in patients with hepatitis B virus infection: A systematic review and meta-analysis. *World J Hepatol* 2018; 10(2): 337-346 Available from: URL: <http://www.wjgnet.com/1948-5182/full/v10/i2/337.htm> DOI: <http://dx.doi.org/10.4254/wjh.v10.i2.337>

## INTRODUCTION

Hepatitis B virus (HBV) infection is one of the most common infectious diseases and major health problems worldwide<sup>[1-3]</sup>. In 2017, approximately 257 million people have chronic hepatitis B virus infection<sup>[1]</sup>. Despite advances in medicine which have resulted in a cure for hepatitis C infection in recent years<sup>[4]</sup>, chronic HBV infection is still currently considered as an incurable disease<sup>[2,3,5]</sup>, leading to significant mortality (887000 death in 2015) and morbidities including cirrhosis and hepatocellular carcinoma<sup>[1,2]</sup>.

Advances in immunosuppression and kidney transplant techniques have led to significant improvements in short-term survival of the renal allograft<sup>[6]</sup>. Long-term graft survival, however, has remained relatively lagged behind and has now become one of the main problems in kidney transplantation<sup>[7-9]</sup>. Although HBV is preventable disease by HBV vaccine, HBV infection remains a challenge issue in patients with end-stage renal disease on dialysis, affecting from 1.3% up to 14.6% of chronic dialysis patients [hepatitis B surface antigen (HBsAg) – positive] depending on geographical regions<sup>[10-12]</sup>, and, consequently leading to chronic HBV infection kidney transplant patients<sup>[13-31]</sup>. Among renal transplant patients with HBV (HBsAg positive), there have been reported cases of HBV reactivation<sup>[32]</sup>, massive liver necrosis due to fulminant hepatitis, and severe cholestatic hepatitis after kidney transplantation<sup>[10,16,33-36]</sup>. In addition, chronic HBV infection may result in HBV-related membranous nephropathy after kidney transplantation<sup>[37-43]</sup>.

Even though HBV is incurable, current more available antiviral agents against HBV effectively suppress viral replication<sup>[10]</sup>. Thus, these agents can prevent hepatic fibrosis<sup>[10]</sup> and potentially reduce significant hepatic and extra-hepatic complications related to chronic HBV. In spite of improvement of HBV care, outcomes of kidney transplantation including patient and allograft outcomes in recipients with HBV infection remain unclear. Thus, we conducted this meta-analysis to (1) Assess the risks of mortality and allograft failure in kidney transplant recipients with HBsAg-positive status; and (2) evaluate trends of patient's outcomes overtime.

## MATERIALS AND METHODS

### Literature review and search strategy

The protocol for this meta-analysis is registered

with PROSPERO (International Prospective Register of Systematic Reviews; no. CRD42017080657). A systematic literature search of MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews from database inception to October 2017 was conducted to identify studies assessing outcomes of kidney transplantation including patient and allograft outcomes in patients with HBV. The systematic literature review was undertaken independently by two investigators (C.T. and W.C.) applying the search approach that incorporated the terms of "hepatitis B" or "HBV", or "viral hepatitis" and "kidney transplantation" which is provided in online supplementary data 1. No language limitation was applied. A manual search for conceivably relevant studies using references of the included articles was also performed. This study was conducted by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement<sup>[44]</sup> and previously published guidelines<sup>[45,46]</sup>.

### Selection criteria

Eligible studies must be randomized controlled trials or observational studies including cohort studies, case-control, or cross-sectional that assessed the risks of mortality and/or allograft loss after kidney transplantation in patients with HBV (HBsAg-positive). They must provide the effect estimates odds ratios (OR), relative risks (RR), or hazard ratios (HR) with 95%CI. The comparison group consisted of HBsAg-negative kidney transplant recipients. Retrieved articles were individually reviewed for their eligibility by the two investigators (C.T. and W.C.) noted previously. Discrepancies were discussed and resolved by mutual consensus. Newcastle-Ottawa quality assessment scale was used to appraise the quality of study for case-control study and outcome of interest for cohort study<sup>[47]</sup>. The modified Newcastle-Ottawa scale was used for cross-sectional study<sup>[48]</sup>, as shown in Table 1.

### Data abstraction

A structured data collecting form was used to derive the following information from each study including title, year of the study, name of the first author, publication year, country where the study was conducted, demographic and characteristic data, mean age, patient's sex, donor type, % of patients with HBsAg, % of patients with coexist patients infected with hepatitis C virus, and adjusted effect estimates with 95%CI and covariates that were adjusted in the multivariable analysis.

### Statistical analysis

Comprehensive Meta-analysis (version 3; Biostat Inc) was used to analyze the data. Adjusted point estimates from each study were consolidated by the generic inverse variance approach of DerSimonian and Laird, which designated the weight of each study based on its variance<sup>[49]</sup>. Given the likelihood of increased inter-observation variance; a random-effect model was

utilized to assess the pooled prevalence and pooled OR with 95%CI for the risks of atrial fibrillation with sleep duration, insomnia, and frequent awakening. Cochran's Q test and  $I^2$  statistic were applied to determine the between-study heterogeneity. A value of  $I^2$  of 0-25% represents insignificant heterogeneity, 26%-50% represents low heterogeneity, 51%-75% represents moderate heterogeneity, and > 75% represents high heterogeneity<sup>[50]</sup>. The presence of publication bias was evaluated via the Egger test<sup>[51]</sup>.

## RESULTS

A total of 1673 potentially eligible articles were identified using our search strategy. After the exclusion of 1639 articles based on the title and abstract for clearly not fulfilling inclusion criteria on the basis of the type of article, study design, population or outcome of interest, leaving 34 articles for full-length review. Eighteen of them were excluded from the full-length review as they did not report the outcome of interest while six articles were excluded because they were descriptive studies without comparative analysis. Thus, the final analysis included 10 cohort studies<sup>[18,21,31,36,52-57]</sup> with 87623 kidney transplant patients. The literature retrieval, review, and selection process are demonstrated in Figure 1. The characteristics and quality assessment of the included studies are presented in Table 1. Patients in most included studies used calcineurin inhibitor-based immunosuppression. Mean age was between the ages of 32-49.

### Mortality after kidney transplantation in patients with HBsAg-positive vs HBsAg-negative status

Ten studies assessed the mortality risk after kidney transplantation in patients with HBV as shown in Table 1. Compared to *HBsAg-negative* patients, *HBsAg-positive* status was significantly associated with increased risk of mortality after kidney transplantation (pooled OR = 2.48; 95%CI: 1.61-3.83,  $I^2 = 82$ , Figure 2). When meta-analysis was limited only to non-HCV patient population, the pooled OR of mortality was 2.98 (95%CI: 1.47-6.07,  $I^2 = 89$ ). When meta-analysis was limited only to studies with adjusted analysis for confounders<sup>[36,53,54]</sup>, the pooled OR of mortality was 1.27 (95% CI: 1.06-1.51,  $I^2 = 85$ ). Meta-regression showed significant negative correlations between mortality risk after kidney transplantation in HBsAg-positive patients and year of study (slopes = -0.062,  $P = 0.001$ , Figure 3). Meta-regression showed no significant impact of donor type on the association between HBsAg-positive status and increased risk of mortality after kidney transplantation ( $P = 0.11$ ).

### Impact of antiviral treatments on patient survival after kidney transplantation in patients with HBsAg-positive

Of 10 studies<sup>[18,21,31,36,52-57]</sup>, 3 studies<sup>[18,21,54]</sup> provided data on prophylactic antiviral treatment for HBV. When meta-analysis was limited only to studies with HBsAg-positive

Table 1 Main characteristics of the studies assessing outcomes of kidney transplantation in patients with hepatitis B virus

Study	Lee <i>et al.</i> <sup>[55]</sup>	Breitenfeldt <i>et al.</i> <sup>[56]</sup>	Chan <i>et al.</i> <sup>[21]</sup>	Morales <i>et al.</i> <sup>[71]</sup>	Ridruejo <i>et al.</i> <sup>[52]</sup>	Aroldi <i>et al.</i> <sup>[53]</sup>	Yap <i>et al.</i> <sup>[16]</sup>	Reddy <i>et al.</i> <sup>[54]</sup>	Grenha <i>et al.</i> <sup>[51]</sup>	Lee <i>et al.</i> <sup>[54]</sup>
Country	Taiwan	Germany	Hong Kong	Spain	Argentina	Italy	Hong Kong	USA	Portugal	Korea
Study design	Cohort study	Cohort study	Cohort study	Cohort study	Cohort study	Cohort study	Cohort study	Cohort	Cohort study	Cohort study
Year	2001	2002	2002	2004	2004	2005	2010	2011	2015	2016
Total number	477	927	509	3365	231	541	126	75681	2284	3482
Age (yr)	38.6 ± 11.5	41.7	N/A	45.6 ± 13.0	38	31.7	49.2	N/A	44.3	40.6 ± 12.9
Male	280 (58.7%)	595 (64.2%)	N/A	2119 (63.0%)	136 (58.9%)	322 (59.5%)	90 (71.4%)	45249 (59.8%)	1524 (66.7%)	2084 (59.9%)
Living donor	N/A	19 (2.0%)	N/A	N/A	N/A	62 (11.5%)	41 (32.5%)	32096 (42.4%)	80 (3.5%)	2571 (73.8%)
HBsAg	62 (13.0%)	37 (4.0%)	67 (13.2%)	76 (2.2%)	17 (7.3%)	77 (14.2%)	63 (50%)	1346 (1.8%)	76 (3.3%)	160 (4.6%)
HBsAg in HBsAg (+) patients	N/A	11/37 (29.7%)	29/67 (43.3%)	N/A	N/A	34/77 (44.2%)	16/63 (25.4%)	N/A	N/A	N/A
HBV treatment	N/A	N/A	Lamivudine	N/A	N/A	N/A	Lamivudine	N/A	N/A	Not specified
Anti-HCV	151 (31.7%)	130 (14.0%)	0 (0%)	513 (15.2%)	106 (45.9%)	244 (45.1%)	0 (0%)	0 (0%)	113 (4.9%)	129/160 (81%)
Immunosuppression	Cyclosporine, steroid, azathioprine, MMF	N/A	Cyclosporine, steroid, azathioprine	Cyclosporine, steroid, azathioprine, MMF, FK506	Cyclosporine, steroid, azathioprine	Cyclosporine, steroid, azathioprine	Cyclosporine/tacrolimus, steroid, MMF	Cyclosporine/tacrolimus, steroid, azathioprine, MMF, mTOR	N/A	Cyclosporine/tacrolimus, steroid, azathioprine/MMF
Follow-up after KTx	6.0 ± 7.0 yr	9.2 ± 4.4 yr	82 ± 58 mo	N/A	39.9 (1-104.2) mo	11 yr	140.1 mo	1098 d	10 yr	89.1 ± 54.1 mo
Mortality	Overall 2.72 (1.48-4.99) No HCV 4.61 (2.41-8.84)	Overall 4.08 (2.10-7.93) No HCV 3.60 (1.72-7.54)	No HCV 8.07 (3.65-17.86)	Overall 2.06 (1.24-3.40) No HCV 2.97 (1.66-5.33)	Overall 2.20 (0.57-8.34)	Overall 2.36 (1.50-3.70) No HCV 4.40 (2.06-9.41)	No HCV 11.70 (1.45-94.40)	Overall 1.07 (0.88-1.31) Living donor 0.98 (0.59-1.63) Deceased donor 1.09 (0.88-1.36)	Overall 1.33 (0.78-2.29) No HCV 1.02 (0.54-1.94)	Overall 1.57 (0.99-2.49) No HCV 1.63 (0.98-2.71)
Graft failure	Overall 1.84 (1.08-3.15) No HCV 3.56 (1.89-6.71)	Overall 2.07 (1.06-4.05) No HCV 1.48 (0.71-3.08)	No HCV 1.61 (0.86-3.03)	Overall 0.62 (0.37-1.02) No HCV 0.59 (0.32-1.09)	Overall 5.45 (1.95-15.23)	Overall 1.55 (1.12-2.14) No HCV 0.65 (0.27-1.54)	N/A	Overall 1.02 (0.81-1.28) Living donor 0.90 (0.62-1.30) Deceased donor 1.10 (0.82-1.47)	Overall 1.38 (0.55-3.50)	
Confounder adjustment	None	None	None	None	None	Age, Hepatitis C status	none	Recipient age, gender, BMI, race, comorbid, dialysis duration, donor HbA1c, expanded criteria donor, HLA DR mismatch, cold ischemia time, induction therapy, immunosuppressants	none	Age, sex, DM, BMI, primary renal disease, donor type, hypertension, ischemic heart disease, immunosuppressive agents
New Castle-Ottawa score	S4 C0 O3	S4 C0 O3	S4 C0 O3	S4 C0 O3	S4 C0 O3	S4 C1 O3	S4 C0 O3	S4 C2 O3	S4 C0 O3	S4 C2 O3

FK506: Tacrolimus; HBsAg: Hepatitis B surface antigen; HBeAg: Hepatitis B e antigen; HCV: Hepatitis C virus; KTx: Kidney transplantation; MMF: Mycophenolate mofetil; S, C, O: Selection, comparability, and outcome.



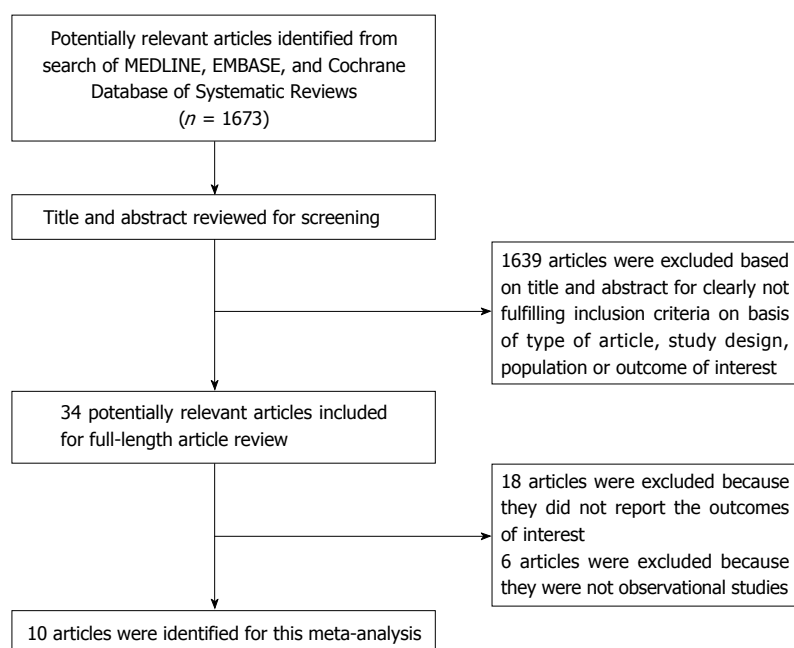


Figure 1 Literature review process.

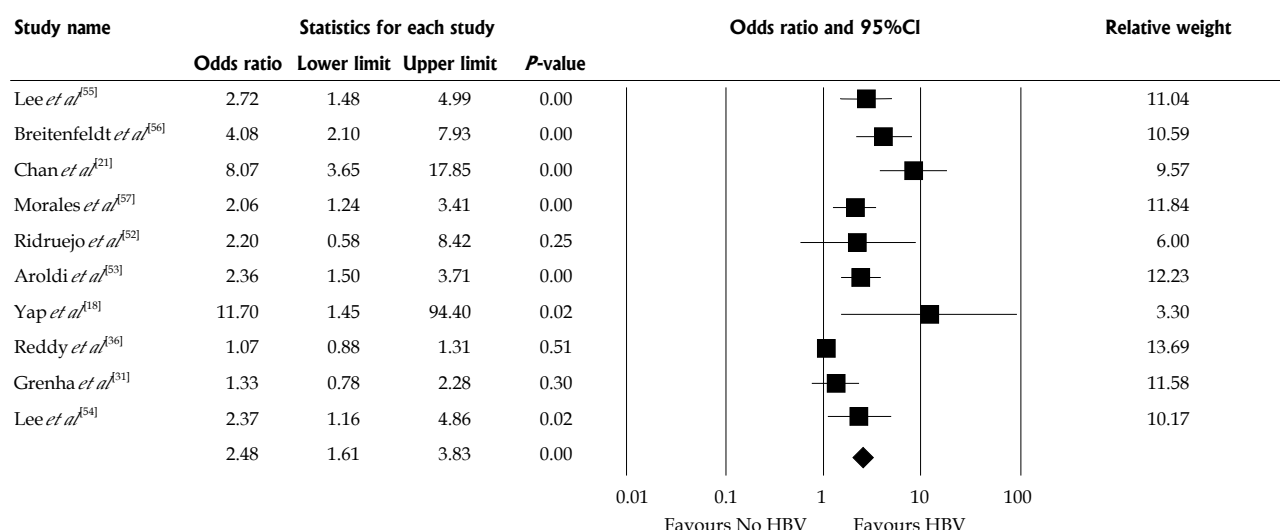


Figure 2 Forest plots of included studies evaluating mortality after kidney transplantation in patients with hepatitis B surface antigen-positive vs hepatitis B surface antigen-negative.

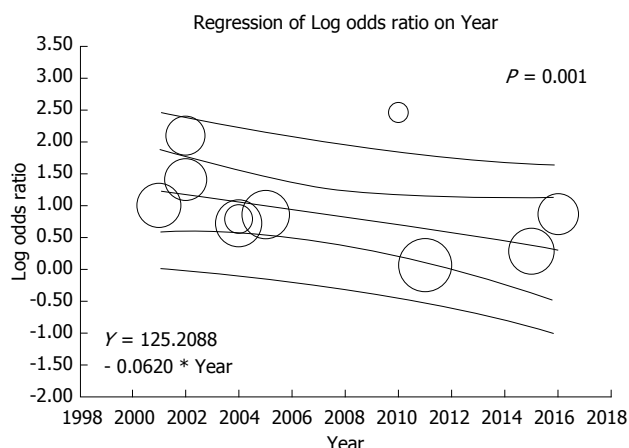
recipients (> 50%) treated with prophylactic antiviral treatment for HBV, the pooled OR of mortality was 3.85 (95%CI: 0.91-16.23,  $I^2 = 50\%$ ). In a recent study by Lee *et al.*<sup>[54]</sup>, which 81% of HBs Ag-positive recipients were treated with prophylactic antiviral treatment, HBsAg-positive status was significantly associated with increased risk of mortality after kidney transplantation with adjusted HR of 2.37 (95%CI: 1.16-4.87).

Yap *et al.*<sup>[18]</sup> demonstrated that recipients treated with nucleoside/nucleotide analogues had significantly better patient survival, when compared to those who were not on treatment (83% vs 34% at 20 years,  $P = 0.006$ ). In patients who had lamivudine-resistant HBV, the investigators showed that treatment with adefovir

or entecavir was effective with a three-log reduction in HBV DNA by 6 mo. When compared to patients who were treated with lamivudine or adefovir, Lee *et al.*<sup>[54]</sup> demonstrated that those treated with new generation antiviral agent entecavir had better patient survival (log-rank,  $P = 0.050$ ).

#### Renal allograft failure in patients with HBsAg-positive vs HBsAg-negative

There were 9 studies assessed renal allograft outcomes in HBsAg-positive patients (Table 1). HBsAg-positive status was significantly associated with increased risk of renal allograft loss with pooled OR of 1.46 (95%CI: 1.08-1.96,  $I^2 = 69$ , Figure 4). When meta-analysis was



**Figure 3** Graphical display of significant negative correlations between mortality risk after kidney transplantation in hepatitis B surface antigen-positive patients and year of study.

limited only to non-HCV patient population, the pooled OR of allograft failure was 1.33 (95%CI: 1.00-1.77,  $I^2 = 80$ ). When meta-analysis was limited only to studies with adjusted analysis for confounders<sup>[36,53,54]</sup>, the pooled OR of allograft failure was 1.25 (95%CI: 0.90-1.73,  $I^2 = 54$ ). There was also a significant negative correlation between year of study and risk of allograft failure (slopes = -0.018,  $P = 0.002$ , Figure 5). Meta-regression showed no significant impact of donor type on the association between HBsAg-positive status and increased risk of renal allograft loss ( $P = 0.52$ ).

### Evaluation for publication bias

We found no publication bias as assessed by the funnel plots (Supplementary Figures 1 and 2) and Egger's regression asymmetry test with  $P = 0.18$  and  $0.13$  for the risks of mortality and allograft failure after kidney transplantation in HBV infected patients, respectively.

## DISCUSSION

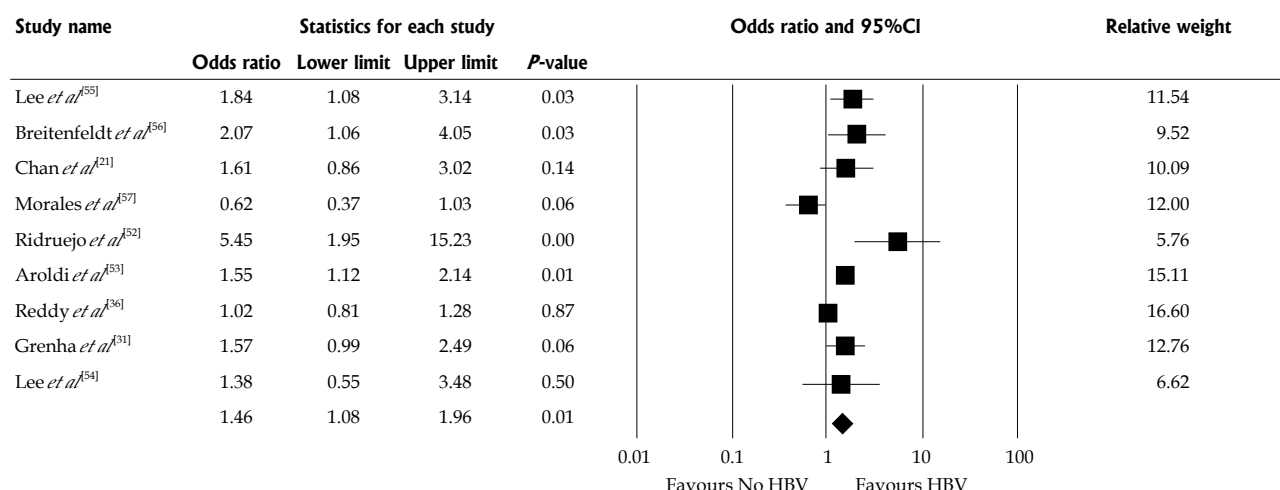
In this systematic review, we demonstrated that HBsAg-positive status in kidney transplant recipients was significantly associated with poor outcomes after transplantation including a 2.5-fold increased risk of mortality and 1.5-fold increased risk of allograft loss. These associations existed in overall analysis as well as in limited cohort of hepatitis C virus-negative patients.

Chronic HBV infection can negatively impact the clinical outcomes of kidney allograft recipients. Compared to the HBsAg-negative recipients, HBsAg-positive recipients carry a higher risk of hepatic complications including chronic hepatitis, liver failure, fibrosing cholestatic hepatitis, and hepatocellular carcinoma<sup>[34,36,58]</sup>. In addition, some immunosuppressive agents after kidney transplantation may also put patients at higher risks of HBV reactivation<sup>[23,40]</sup>. HBV genome contains glucocorticoid responsive element that activates transcription of HBV genes<sup>[35]</sup>. Moreover, cyclosporine may also enhance HBV replication, leading

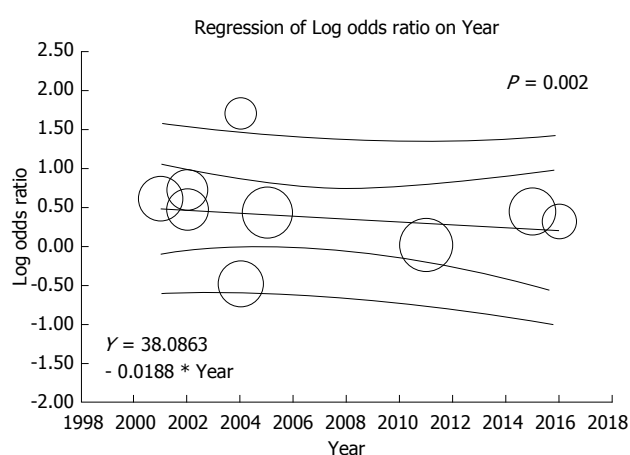
to higher risks of HBV-related complications in kidney transplant recipients<sup>[37]</sup>. Previously, in 2005, Fabrizi *et al.*<sup>[27]</sup> conducted a meta-analysis of six observational studies and demonstrated a significant association between HBsAg seropositive status and increased mortality after kidney transplantation. Since then, although hepatitis B is still incurable, there have been significant advancements in antiviral agents including the United States Food and Drug Administration approvals of entecavir in 2005 and telbivudine in 2006<sup>[59]</sup> resulting in reasonably sustained suppression of HBV replication after kidney transplantation<sup>[10]</sup>. Our meta-analysis with a new era of medicine also demonstrated a 2.7-fold increased risk of mortality in kidney transplant recipients with HBsAg positivity, when compared to HBsAg-negative recipients. In addition, our meta-analysis is the first to demonstrate a significant negative correlation between the mortality risk and year of study, which potentially represents improvements in patient care and management for chronic HBV in kidney transplant patients<sup>[60]</sup>. Although antiviral treatment has been shown to reduce mortality after kidney transplantation due to decrease in liver complications<sup>[18,21,54]</sup>, in the era of antiviral therapies, Lee *et al.*<sup>[54]</sup> recently showed that deaths from liver complications remained a significant problem accounting for 40% of deaths in HBsAg patients and 22.2% of all mortalities that occurred in recipients treated with antiviral agents<sup>[54]</sup>.

There are several plausible explanations for the increased risk of renal allograft failure in recipients with HBsAg-positivity. Firstly, it is known that chronic HBV infection can result in HBV-related membranous nephropathy, not only in patients with native kidneys but also in kidney transplant recipients<sup>[37-43]</sup>. Secondly, due to a concern of HBV reactivation, physicians may avoid or limit the use particular immunosuppression or Rituximab in HBsAg-positive patients when it is indicated such as for recurrent glomerulonephritis post-transplantation<sup>[61,62]</sup>. Lastly, treatment of chronic HBV infection itself such as tenofovir could affect renal function<sup>[63]</sup>. Thus, the findings from our meta-analysis confirm an increased risk of allograft failure in HBsAg seropositive patients, when compared to HBsAg-negative recipients. Also, we found a significant negative correlation between the risk of allograft failure in HBsAg positive patients and year of study. Recently, data analysis from the Organ Procurement Transplant Network/United Network for Organ Sharing database (OPTN/UNOS) suggested no increased risk for allograft failure or death in HBV-infected kidney transplant patients in a recent era (between 2001 and 2007)<sup>[36]</sup>. Although follow-up time was limited to only 3 years post-transplant, these data along with the findings from our study suggest potential improvements in patient and graft survivals in HBsAg-positive recipients overtime.

There are several limitations in this meta-analysis that bear mentioning. First, there was low to moderate statistical heterogeneity between studies in meta-



**Figure 4** Forest plots of included studies evaluating renal allograft failure in patients with hepatitis B surface antigen-positive vs hepatitis B surface antigen-negative.



**Figure 5** Graphical display of a significant negative correlation between year of study and risk of allograft failure.

analysis assessing the risks of mortality and allograft failure in HBsAg-positive recipients. The possible source of this heterogeneity includes the difference in population, type of donor, number of patients with positive HBeAg, immunosuppression regimens, and difference in confounder adjustments. In addition, the data on the graft quality (e.g., Kidney Donor Profile Index) and surgical technique in HBsAg-positive recipients were limited. Second, despite the associations of HBsAg-positive status with poor kidney transplant outcomes, there is limited evidence whether the treatment with antiviral drugs for chronic HBV helps improve patient and allograft survival. However, with potential improvements in patient and graft survivals overtime demonstrated in our meta-analysis, future studies are required to evaluate if advancement in patient care for chronic HBV plays an important role. Also, additional studies are required to identify optimal antiviral treatment regimens and duration of suppressive therapy for HBV after kidney transplantation, since outcomes after withdrawal of antiviral treatment in

kidney transplant recipients with chronic HBV infection remain unknown. While cautious withdrawal of antiviral therapy post kidney transplantation has been described especially in those with stable renal allograft function, low immunological risk for rejection and no evidence for HBV activity<sup>[10,23]</sup>, fatal hepatitis flares in several kidney transplant recipients have been reported after withdrawal of antiviral therapy<sup>[64]</sup>. Lastly, this is a meta-analysis of observational studies. Thus, it can at best identify only associations of HBsAg-positive status with poor kidney transplant outcomes, but not a causal relationship.

In summary, our study reveals an association between HBsAg-positive status in kidney transplant recipients and higher risks of mortality and allograft failure after kidney transplantation. However, there are also significant negative correlations between the risks of mortality and allograft failure and year of study, representing potential improvements in patient and graft survivals overtime.

## ARTICLE HIGHLIGHTS

### Research background

Among renal transplant patients with hepatitis B virus (HBV) (HBsAg positive), there have been reported cases of HBV reactivation, massive liver necrosis due to fulminant hepatitis, and severe cholestatic hepatitis after kidney transplantation. In spite of improvement of HBV care, the outcomes of kidney transplantation including patient and allograft outcomes in recipients with HBV infection remain unclear.

### Research motivation

Although hepatitis B is still incurable, there have been significant advancements in antiviral agents resulting in reasonably sustained suppression of HBV replication after kidney transplantation. The results of studies on kidney transplant outcomes in patients with renal transplant patients with HBV (HBsAg positive) were inconsistent. To further investigate outcomes of renal transplant patients with HBsAg positivity, the authors conducted this systematic review and meta-analysis reporting the association between HBsAg positivity in kidney transplant recipients and higher risks of mortality and allograft failure after kidney transplantation.

## Research objectives

We conducted this meta-analysis to assess the outcomes of kidney transplantation including patient and allograft outcomes in recipients with HBV infection; and the trends of patient's outcomes overtime.

## Research methods

A literature search was conducted using databases (MEDLINE, EMBASE and Cochrane Database) from inception through October 2017. Those studies reported odds ratios (OR) of mortality or renal allograft failure after kidney transplantation in HBV patients (defined as HBsAg positive) were included. HBsAg-negative kidney transplant recipients are the comparison group. The effect estimates from the individual study were extracted and combined.

## Research results

The authors demonstrated that HBsAg-positive status in kidney transplant recipients was significantly associated with poor outcomes after transplantation. These associations existed in overall analysis as well as in limited cohort of hepatitis C virus-negative patients.

## Research conclusions

The authors found significant associations of HBsAg positive status with poor outcomes after transplantation. Significant negative correlations between the risks of mortality and allograft failure and year of study, representing potential improvements in patient and graft survivals overtime were found.

## Research perspectives

This study demonstrated significantly increased risks of mortality and allograft failure in HBsAg-positive kidney transplant recipients. This finding suggests that HBsAg positive status may be an independent potential risk factor for poor outcomes after transplantation. However, there are also potential improvements in patient and graft survivals with HBV infection overtime.

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**P- Reviewer:** Hilmi I, Lu K    **S- Editor:** Wang JL    **L- Editor:** A  
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